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# Botanical description, Photochemistry, Traditional Uses, and Pharmacology of the "Wonder Plant" Kalanchoe Pinnata (Linn.) Pers: An Updated Review

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**Abstract**

***Background:*** Kalanchoe pinnata, an important medicinal plant of the stonecrop family, is widely distributed in India and tropical and subtropical parts of the world. It has been reported for its folkloric use in various disorders such as abdominal discomfort, boils, bruises, cholera, cuts, diabetes, diarrhea dysentery, flatulence, headaches, kidney stones, indigestion, insect bites, scabies, sores, urinary insufficiency, wounds.

***Results:*** The present review has focused on the botanical description, phytochemistry, and ethnomedicinal and traditional uses of Kalanchoe pinnata along with its reported pharmacological activities. Chief chemical constituents and pharmacological aspects of Kalanchoe pinnata have been deeply explored to unravel the unexplored folklore/ ethnomedicinal uses of this plant so that the researchers working on this plant may be able to find new insights to continue the further investigation on this plant. The pharmacological aspects like anti-diabetic, anti-inflammatory, anti-nociceptive, anti-diarrheal, anti-pyretic, and anti-cancer potentials evaluated by various in vitro/in vivo methods on this plant have been reported.

***Conclusion:*** Various traditional uses have been reported that need to be scientifically investigated in-depth and several pharmacological activities have been reported for the Kalanchoe pinnata, but more detailed and mechanism-based studies linked to a particular lead compound need to be targeted in the future. Moreover, this plant has not been completely assessed based on its safety and efficacy in humans. It is expected that this review will compile and improve the existing knowledge on the potential utilization of Kalanchoe pinnata in complementary and alternative medicine.

**Keywords:** Kalanchoe pinnata, Ethano-Botanical, Traditional, Phytochemistry, Pharmacology.

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## BACKGROUND

The World Health Organization (WHO) defined health as "a complete state of physical, mental, and social well-being and not merely the absence of disease or infirmity."Diseases are at the upward thrust given the appearance of lifestyles on the earth. Procuring a protective mechanism is a task for researchers. In many developing countries a

large proportion of the population relies heavily on traditional practitioners and medicinal.[1] Plants to meet primary health care needs. Plants are a boon to mankind. They are explored, researched, and exploited to fight diverse dreadful illnesses. Plants that show a remedy to illnesses are taken into consideration as medicinal. Their healing nature additionally prevents occurrences of sure conditions. Such plant-primarily based total compounds are much less poisonous and display minimum or nil side effects. Kalanchoe pinnata (Lamarck) Persoon (=Bryophyllum pinnatum) is a perennial medicinal herb, popularly used in Brazil and other parts of the world to treat various inflammatory diseases.[2] It is a succulent perennial plant that grows 1-1.5 m in height. Leaves are opposite, decussate, succulent, 10-20 cm long. They are fleshy dark green that is distinctively scalloped and trimmed in red. The stems are tall and the Flowers are many bell-like pendulous. Calyx tubular, 2-4 cm; Corolla reddish to purple. The fruit pod with four septa and numerous, ellipsoid, smooth striate seeds within. The plant flowers in Nov-Mar and fruits on April.[3]

## MAIN TEXT

### *Geographical description*

This plant is mostly found in plains, tropical and temperate regions of Africa, Australia, and America. It is also widely distributed in the Philippines and it is known as katakataka or kataka-taka which is also an adjective meaning astonishing.[4]

## BOTANICAL DESCRIPTION[5]

Kalanchoe pinnata (Family: stonecrop) having synonyms Bryophyllum calycinum, Bryophyllum pinnatum is commonly known as Zakhm-Hayat (Hindi), kushnulhayat (Arabic), Koppata (Bengal), asthi-bhaksha (Sanskrit), simajamudu (Telgu), ranakalli (Tamil), ganduklinga (Kannad), elamurunga (Malayalam), Chubehay (Persian & Urdu) in different regions of India. Cathedral Bells, Air Plant (USA), Life Plant, Miracle Leaf, Goethe Plant, and Katakataka. Also called "Wonder of the World" in the English-speaking Caribbean. 'Oliwa Ka Kahakai (Hawaii), Mother of Thousands, Herbe Mal Tete (Dominica)Never Dead, Parvu, Hoja Del Aire (Bolivia) in different regions of the world.

***Taxonomy6***

| | |
|---|---|
| Kingdom | Plantae |
| Division | Magnoliophyta |
| Class | Magnoliopsida |
| Order | Saxifragales |
| Genus | Kalanchoe |
| Section | Bryophyllum |
| Species | K. pinnata |

## MACROSCOPIC CHARACTERISTICS

It is a succulent perennial plant that grows 1-1.5 m in height. Leaves are opposite, decussate, succulent, 10-20 cm long. They are fleshy dark green that is distinctively scalloped and trimmed in red. The stems are tall and the Flowers are many bell-like pendulous. Calyx tubular, 2-4 cm; Corolla reddish to purple. The fruit pod with four septa and numerous, ellipsoid, smooth striate seeds within. The plant flowers in Nov-Mar and fruits in April.[7]


**Fig. 1:** Various parts of plant Kalanchoe pinnata[7]

## HISTOLOGICAL CHARACTERISTICS

The microscopic studies of leaves of the plant showed xylem, phloem mesophyll tissue, midrib, while the trichomes were absent on both sides i.e. adaxial side and abaxial side. It is broadly shallow on the adaxial side and convex on the abaxial side. It has a thin adaxial epidermal layer of small, less prominent cells. The abaxial epidermis is also nary thin and less distinct. The ground tissue of the midrib is parenchymatous and homogenous. The cells are circular or angular and compact. The

vascular strand is single, collateral, small, and hemispherical. It consists of a thick horizontal band of xylem and a fairly wide band of phloem.[8] The vascular bundle is 100µm in the vertical plane and 170 µm in the horizontal plane. The lamina is uniformly flat with an even surface. The mesophyll tissue is not differentiated into palisade and spongy parenchyma. The stomata are abundant, these are 18-20 stomata per mm², having anisocytic in nature.[9]

### *Traditional/Ethnomedicinal uses*

Kalanchoe pinnata has long been used to treat healing wounds in traditional medicine to treat psychiatric disorders and as a tocolytic agent to prevent premature labor.[10] The chemical constituents of the plant (flavonoids, polyphenols, triterpenoids, and phytosterols) are speculated to account for the antinociceptive, anti-inflammatory, and antidiabetic activities of the herb's leaf aqueous extract.[11] The juice from fresh leaves is used to treat vomiting, earache, smallpox, otitis, cough, asthma, bronchial disorders, diarrhea, blood dysentery, jaundice, gout, headache, convulsion, and general debility.[12] It is also used for the treatment of jaundice in folk medicines of the Bundelkhand region of India. (rajsakhar). The leaf juice is used for the treatment of ear infections, cough, and dysentery Among the Yoruba tribe of south-western Nigeria, the crushed leaves are rubbed on or tied to the head to bring relief to Headache.[13]

**Table1:** Traditional uses of Kalanchoe pinnata

Worldwide Ethnomedical Uses 17

| | | |
|---|---|---|
| **In India** | For abdominal discomfort, boils, bruises, cholera, cuts, diabetes, diarrhea, dysentery, flatulence, headaches, kidney stones, indigestion, insect bites, scabies, sores, urinary insufficiency, wounds | |
| | In Himalaya | Leaves are applied to a wound, bruises, swelling, and insect bite |
| | Arunachal Pradesh | Leaf extract is taken on an empty stomach is used in the treatment of urinary bladder stones and fewer in children's. |
| | Orisaz | For diarrhea |
| | Maharashtra | The leaves juice is used against cough, dysentery |
| | Karnataka | Leaf juice is externally applied to scabies and leucoderma and a leaf decoction is applied over cuts to stop bleeding. |
| | Bundelkhand | Juice of the fresh leaves is used very effectively for the treatment of Jaundice. |
| | Kerala | plants species are used for treating cancer symptom |
| Outside India | Mexico | For eye infections, headaches, inflammation, menstrual disorders, pimples, wounds |
| | Nicaragua | For aches, burns, childbirth, colds, coughs, fever, headache, pain, respiratory infections |
| | Nigeria | For coughs, earaches, eczema, inflammation, pimples |
| | Peru | For bacterial infections, boils, broken bones, bronchitis, cancer (lymphoma), conjunctivitis, coughs, earaches, eye infections, epilepsy, erysipelas, fever, gas, headache, heartburn, inflammation, intestinal problems, migraine, nausea, skin problems, sores, ulcers, urethritis |
| | Bangladesh | For coughs, mucus, fever, epilepsy, constipation, piles, etc |
| | South America | For asthma, chest colds, earaches, headaches, sores, strains, tumors |
| | USA | For chickenpox, fevers, stomachache |
| | West Indies | For menstrual disorders, ulcers, hypertension, urinary disorder |
| | Vietnam | For antibacterial and anti-inflammatory |
| | Elsewhere | For arthritis, asthma, bruises, burns, constipation, diabetes, earaches, headaches, malnutrition, migraines, nephritis, paralysis, respiratory infections, rheumatism, sprains, swelling, ulcers, wounds, and induce vomiting of blood cut the umbilical cord in newborn baby, expel worms. |
| | Brazil | For abscesses, adenoids(infected), arthritis, athlete's foot, boils, bronchitis, buboes, burns, calluses, conjunctivitis, corns, coughs, dermatitis, dermatosis, earaches, eczema, edema, erysipelas, fever, glaucoma, headache, infections, inflammation, insect stings, intestinal problems, itch, kidney stones, lymphatic disorders, mouth sores, nervousness, respiratory infections, rheumatism, scurvy, skin problems, toothache, tuberculosis, tumor, ulcers, urinary insufficiency, wart, whooping cough, wounds, and as a sedative. |
| | Ecuador | For bruises, broken bones |
| | Guatemala | For aches, diarrhea, pain, skin problems |
| | Southeastern Nigeria | herb is used to facilitate the dropping of the placenta of a newborn baby |

## PHYTOCHEMISTRY

Kalanchoe pinnata is rich in glycosides, alkaloids, flavones, triterpenoids, cardenolides, and bufadienolides. Bufadienolides are present in the leaves. Bufenolides are similar in structure to cardenolides and possess anticancer, insecticidal, and antibacterial action. The occurrence and biological significance of main phytoconstituents is discussed below.

### *Phenols, Phenylpropanoids, and Flavanoids:*

Leaves contain astragalin, 3,8-dimethoxy-4,5, 7-trihydroxyflavone, friedelin, epigallocatechin -3-osyringate, luteolin, rutin, kaempferol , quercetin, quercetin-3 L-rhamonsido -L-arabino furanoside; quercetin-3-Odiarabinoside, kaempferol- 3-glucoside, kaempferol - 3-O-α-L- arabinopyranosyl (1→2)α –L rhamno pyranoside, quercetin-3-O-α-L-arabino pyranosyl (1→2)α -L-rhamno pyranoside and 4', 5- dihydroxy- 3', 8-dimethoxy flavone-7O- β- Dglucopyranoside. 5,6,7,8,4' pentahydroxy flavanone. 1-Octen-3-O-α-L-arabinopyranosyl-(1-6)-β-glucopyranoside, Quercetin glucose rhamnose, Quercetin glucose arabinose rhamnose, Isorhamnetin hexose pentose, Isorhamnetin derivative pentose, deoxyhexose, Quercetin 3-O-α-l-arabinopyranosyl (1→2) α-L-rhamnopyranoside.[14]

### *Fatty Acids, amino acids, proteins, and vitamins*

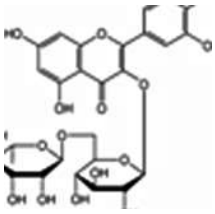
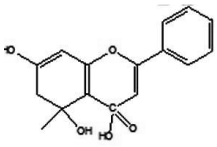
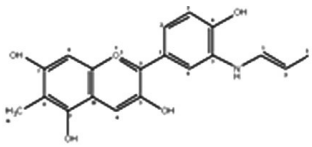
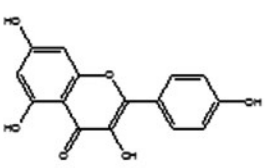
Saturated fatty acids like palmitic acid, stearic acid, behenic acid, and polyunsaturated fatty acids like arachidic are present in this plant. The plant also contains vitamin B-complex (B1,B2,B3,B6) including vitamin –c. an amino acid sulfur group-containing amino acids cysteine, methionine Aliphatic amino acid glycine aromatic amino acid tryptophan protein casein.[15]

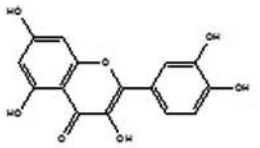
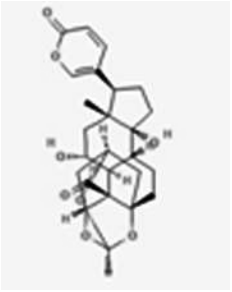
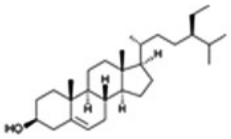
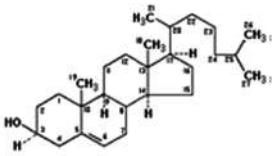
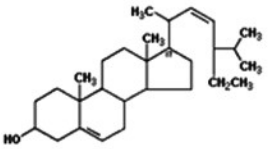
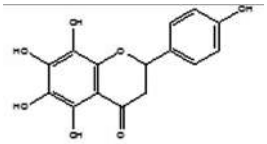
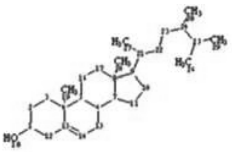
## MINERALS AND CARBOHYDRATES

The herb is a good source of macro and micro mineral elements such as Na, Ca (96.5µg/g) K (76.40µg/g), P(26.42mg/100) Mg, Mn, Fe, Cu, Zn. Carbohydrates contain polysaccharides raffinose, Disaccharides lactose, sucrose, monosaccharides glucose, galactose, fructose. The plant also contains HCN, oxalic acid, citric acid, isocitric acid, oxaloacetate, malic acid, and succinic acid.[16]

## TRITERPENOIDS AND STEROIDS

The cardenolides and steroidal contents include β-sitosterol, bryophyllol, bryophynol, bryophyllin B (Antitumor), bryophyllin A (bryotoxin C,bufadienolide1,3, 5-orthoacetate) with potent cytotoxicity, an insecticidal bufadienolide bryophyllin C and bersaldegenin-3-acetate, bryotoxin A, bryotoxin B. amyrin, amyrinacetate, amyrin, amyrinacetate _-β sitosterol with potent cytotoxicity, an insecticidal action.[17]

| Name of Compound | Structure | Iupac name | Chemical class |
|---|---|---|---|
| Rutin |  | 2-(3, 4 - dihydroxyphenyl)-5, 7-dihydroxy - 3 - [(2S, 3R, 4S, 5S, 6R)-3, 4, 5-trihydroxy - 6 - [[(2R, 3R, 4R, 5R, 6S)-3, 4, 5-trihydroxy - 6 - methyloxan - 2-yl]oxymethyl] oxan - 2 - yl] oxychromen-4-one | Flavonol glycoside[18] |
| ----- |  | 5 Methyl 4, 5, 7 trihydroxyl flavone | Flavanoid[19] |
| ----- |  | 4, 3, 5, 7 tetrahydroxy 5-methyl 5-propanamide Anthocyanidins | Glycoside[20] |
| Kaempferol |  | 3, 5, 7 - trihydroxy - 2 - (4 - hydroxypheny) chrome | Flavone[21] |

| | | | |
|---|---|---|---|
| Quercetein |  | 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxychromen-4-one | Flavonoid[22] |
| Bryophyllin A |  | (1S,4R, 5S,8R, 9R,11R, 12S, 13R, 14R, 16R, 18S) - 5, 11-dihydroxy-9, 16-dimethyl-8- (6-oxopyran-3-yl)- 15, 17, 20-trioxahexacyclo [14.3.1.114, 18.01, 13.04, 12.05,9] henicosane-13-carbaldehyde | Flavonoid[22] |
| Beta-Sitosterol |  | (3S, 8S, 9S, 10R, 13R, 14S, 17R)-17-[(2R,5R)-5-ethyl-6-methylheptan-2-yl] -10,13-dimethyl -2, 3, 4, 7, 8, 9, 11, 12, 14, 15, 16, 17-dodecahydro-1H-cyclopenta [a] phenanthren-3-ol | Phytosterols[22] |
| Cholestrol |  | (3β)-cholest-5-en-3-ol | Animal sterol[23] |
| Stigmasterol |  | (3S, 8S, 9S, 10R, 13R, 14S, 17R)-17- [(E, 2R, 5S)-5-ethyl-6-methylhept - 3-en-2-yl] - 10,13-dimethyl - 2, 3, 4, 7, 8, 9, 11, 12, 14, 15, 16, 17-dodecahydro-1 H-cyclopenta [a] phenanthren-3-ol | Steroid[24] |
| --------- |  | 5, 6, 7, 8, 4' pentahydroxy flavanone | Flavanone[25] |
| Campesterol |  | (3S, 8S, 9S, 10R, 13R, 14S, 17R)-17- [(2R, 5R)-5,6- dimethylheptan - 2-yl] - 10, 13-dimethyl-2, 3, 4, 7, 8, 9, 11, 12, 14, 15, 16, 17-dodecahydro-1H-cyclopenta [a] phenanthren-3-ol | Steroid[26] |

## PHARMACOLOGICAL ACTIVITIES

Owing to its widespread traditional and medicinal uses, Kalanchoe pinnata has been subjugated for various pharmacological activities as mentioned below.

## ANTIDIABETIC ACTIVITY

Diabetes is a major risk for cardiovascular diseases such as stroke, and heart attack which affect the majority of the global population. The hypoglycaemic efficacy of the plant's aqueous extract by producing diabetes in rats with streptozotocin. The drop in blood glucose level was noticed after the aqueous extract was taken orally. After 24 hours of continuous observation, the glucose levels returned to normal baseline levels, showing the plant's anti-diabetic potential.[27] K. pinnata's ethanolic extract has anti-diabetic properties and the activity is influenced by the habitat of the plant. The drier the climate, the stronger the activity will be. The sunlight can improve flavonoid constituents in the plant as a result of adaptation because of the near wavelength effect of the sunlight. Temperature and water supply at certain seasons can also influence

flavonoid constituents in leaves.[28] The DCM (Di chloromethyl) fraction of the plant demonstrated glucose-independent insulin secretagogue action similar to the currently used drug glibenclamide and hence needs to be administered just before meals as in the case of glibenclamide.[29] K. pinnata Aquos extract demonstrated a decrease in body weight and hypoglycemic and hypocholesterolemic activities which are beneficial in the management of diabetes. The decrease in blood glucose may be due to the increased glycolytic pathway in the liver as shown by the elevated pyruvate kinase activity.[30] A fraction of ethanolic extract of plant leaves was orally administered to male rats. The bioactive compound responsible for antihyperglycemic action was subjected to column chromatography and it was confirmed as flavonoids after spectral analysis. it lowers the blood glucose level significantly ($P<0.05$) in diabetic rats.[31] The antidiabetic activity of ethanolic and aqueous extracts of the dried stem of K. pinnata against alloxan-induced diabetes in rats. Both the extracts exhibited hypoglycemic activity, that is, significant antihyperglycemic activity. The activities of both the extracts were compared and it was observed that the ethanolic extract showed more inhibitory activity of α-amylase enzyme than the aqueous extract, while the aqueous extract showed more hypoglycemic activity than the ethanolic extract but as compared to standard drug metformin they have little activity.[32] Goyal et al evaluated the antihyperglycemic action of ethanolic extract of the plant. The fraction from EEKP was found to lower the blood glucose level significantly ($P<0.05$) in diabetic rats. the compound which was identified and responsible for hypoglycemic action was phenolic compound nature (Flavonoids) confirmed by spectral analysis.[33] The methanolic extract of the plant has been analyzed by (GS-MS) which rivals the presence of 34 compounds that shows alfa glucosidase inhibitor activity and alfa amylase inhibitor activity. Hence the extract is considered to have anti-diabetic properties.[34] The extracts were prepared by decoction (LAED, lyophilized-water:ethanoldecoction) and by infusion (LAEI, lyophilized-water:ethanol-infusion) when given orally to Male Sprague-Dawley rats at doses of 250, 500, and 750 mg/Kg and blood sugar levels were monitored over four hours using a glucometer. A significant reduction ($p < 0.05$) in blood glucose was observed after one hour in rats treated with 500 mg/Kg of LAED extract. Treatment with 750 mg/Kg LAEI induced a statistically significant reduction in blood sugar at 90, 180, and 240 min, showing that the glucose-lowering effect of this extract was greater at a higher concentration Although the extracts did not elicit the same response as the commercial drug glibenclamide, the extracts LAED (500 mg/Kg) and LAEI (750 mg/Kg) induced a positive response in the reduction of blood glucose levels after starch ingestion. The LED (500 mg/Kg) extract showed a more constant glucose reduction over time.[35]

## NEPHROPROTECTIVE ACTIVITY

Aqueous extract of K. pinnata leaves significantly protects rat kidneys from gentamicin-induced histopathological changes. Gentamicin-induced glomerular congestion, peritubular and blood vessel congestion, epithelial desquamation accumulation of inflammatory cells, and necrosis of the kidney cells were found to be reduced in the group receiving the leaf extract of K. pinnata along with gentamicin. This extract also normalized the gentamicin-induced increases in urine and plasma creatinine, blood urea, and blood urea nitrogen levels.[36] (Harlalka et al. 2007) chemically (ethylene glycol) induced urolithiasis in mice to study the nephroprotective effect of K. pinnata. The chemical inhibited protein synthesis, causing tissue damage and increased excretion of protein in the urine. This process may cause severe necrosis of the proximal tubules throughout the cortex and the outer stripe of the medulla Ethylene glycol also damaged the renal tubule and suppressed the excretion of urea in the renal tubule leading to elevated levels of urea in serum. Its disproportionate accumulation in kidney failure contributed to the formation of stones which varied the different biochemical parameters related to renal functions like urea, creatinine, uric acid, total protein, etc. The urea level was decreased and brought back to normalcy, and there was an efficient reduction in the calcium oxalate levels which inhibited stone formation after administration of ethanolic extract of K. pinnata.[37] aqueous extract of Kalanchoe pinnata In combination with alcoholic extract of Aerva javanica, Hydroalcoholic extract of Ocimum basilicum was given to management and treatment of kidney disease. This Polyherbal mixture of selected plants was screened for their nephroprotective activity. Polyherbal mixture of plant shows maximum nephroprotective activity against Vero cell line by induced toxicity with cisplatin.[38] The nephroprotective effect of silver nanoparticles (AgNPs) synthesized by Bryophyllum pinnatum has been evaluated in ethylene glycol-induced urolithiasis in rats. An animal study was performed on male Wistar rats, which demonstrated a significant increase in serum total protein, albumin, and globulin and a significant

decrease in AST, ALT, creatinine, BUN, calcium, and phosphorus No crystalluria was observed in rats given B. pinnatum AgNP he beneficial preventive and therapeutic nephroprotective effect of B. pinnatum mediated AgNPs against ethylene glycol induced urolithiasis in the rat.[39]

## ANTICONVULSANT ACTIVITY

K. pinnata methanolic extracts of root and stem exert anticonvulsant effects in PTZ (Pentyline tetrazole)-induced seizure models. Stem extracts provide total protection against PTZ lethality with the same efficacy as DZP(Diazepam. The metabolites responsible for the stem extract activity are found in the CHCl3and AcOEt fractions, which suggests this activity is due to sterols and terpenes. MRE (methanolic root extract) activity, may be attributable to the presence of sterols.[40]

## WOUND-HEALING ACTIVITY

Animal treated with ethanolic extract exhibited significant wound healing potency when compared with standard drug mupirocin. There was also a significant decrease in edema at the wound site after 3 days of administration of the extract. The hydroxyproline content of granulation tissue was significantly higher compared to animals of the control group.[41]

## OVICIDAL AND LARVICIDAL ACTIVITY

Kalanchoe pinnata leaf crude extracts exhibited ovicidal and larvicidal action against Culex quinquefasciatusThe extracts showed dose-dependent toxicity to Culex quinquefasciatus eggs and larvae. Among the extracts tested, the crude acetone extract of medicinal plant leaves was found to be effective with a hundred percent mortality of eggs at 250 ppm and the LC50 and LC90 values of fourth instar larvae were 199.86 and 387.70 ppm respectively. The finding of the present investigation revealed that the leaf extracts of Kalanchoe pinnata possess remarkable ovicidal and larvicidal activity against medically important vector mosquitoes and this is the low-cost and ideal eco-friendly approach for the control of mosquitoes.[42]

## ANTILEISHMANIAL ACTIVITY

The aqueous extract was given to mice infected with Leishmania amazonensis by oral route exhibiting the significantly delayed onset of disease when compared to untreated animals or animals receiving KP. By intravenous or topical route.[43] Aqueous extract of Kalanchoe pinnata leaf possesses antileishmanial activity Quercetin a flavanoid is a very potent and safe antileishmanial present in this extract which has invitro activity. when compared with standard drugs pentosan quercetin exhibits significant activity With an IC 50 value approx 1µg/ml.[44]

## ANTIALLERGIC ACTIVITY

Aqueous extract of Kalanchoe pinnata (Kp) is effective in mice to reduce acute anaphylactic reactions. Treatment with Kp and QE (quercetin) in vitro inhibited degranulation and cytokine production of bone marrow-derived mast cells following IgE/Fc_RI crosslinking, whereas treatment with QI had no effect. Similarly, in vivo treatment with Kp and QE decreased the development of airway hyperresponsiveness, airway inflammation, goblet cell metaplasia, and production of IL-5, IL-13, and TNF.[45]

## ANTI-INFLAMMATORY AND ANALGESIC ACTIVITY

Swiss albino mice (20-25 g) and albino Wister rats (150-200 g) of either sex were given Ethanolic and Aqueous extract of plant kalanchoe pinnata Both the extracts exhibit anti-inflammatory activity against the carrageenan-induced paw edema in rats. The reductions of paw edema of rats compared with the standard drug i.e. Indomethacin. The same method was applied for The evolution of analgesic action and compared with standard drug pentazocine activity of Higher concentrations of extracts have greater activity than lower ones46. The subcutaneous administration of KP flower aqueous extract (KPFE), its ethyl acetate (EtOAc) and butanol (buohf) fractions, and the main KP flavonoid [quercetin 3-O-L-arabinopyranosyl (1→ 2)-L-rhamnopyranoside] (KPFV) in mice exhibit the antinociceptive, antiedematogenic, and anti-inflammatory action by COX-1/COX-2 and TNF-synthesis/release inhibition.[47] Anti-inflammatory activity possessing bio-compounds was identified from Kalanchoe pinnata methanolic leaf extract using Gas chromatography-mass spectrometry (GC-MS) analysis and their anti-inflammatory potential was checked using inhibition of albumin denaturation assay, anti-proteinase activity assay, and heat and hypotonicity induced hemolysis assay. GC-MS analysis revealed the presence of six bioactive molecules for dock in analysis one

compound (1-Benzyl-3-isopropyl-5-(1-allylindol-3-yl)-5-t-butyloxy carbonylpyrrole-3-one) highest binding affinity toward the COX-2 protein.[48] The analgesic effect of the methanol leaf extract was evaluated by the 'hot-plate' and 'acetic acid' test models of pain in mice. The anti-inflammatory effects of the plant's extract were investigated using Carageenan induced hind paw edema in rats and local anesthetic activity was studied using foot withdrawal reflex in the frog. Methanol extract of the plant showed significant dose depended on analgesic activity up to 83.79% against 'acetic acid' induced pain in mice compared to 97.93% produced by piroxicam and showed mild anti-inflammatory activity up to 43.10% against Carageenan induced hind paw edema in rats compared to 75.66% produced by piroxicam but failed to reveal any analgesic activity against thermal stimuli using hot plate method and did not show any local anesthetic activity49.

## ANTIHELMINTIC ACTIVITY

Petroleum ether and methanolic extracts were investigated for their anthelmintic activity against Pheretima Posthuma. Both the extract even in higher concentrations. No vermicidal activity so it is insignificant for antihelmintic activity.[50]

## ANTIDEPRESSANT ACTIVITY

Central nervous depressant activity exhibited by the ethanolic and aqueous extract of dried stem of plant Kalanchoe pinnata on the locomotor activity of mice using Actophotometer. Alcoholic extract of plant Kalanchoe pinnata has more CNS-depressant activity as compared to aqueous extract but as compared to standard drug chlorpromazine it shows near about the same action.[50]

## ANTIUROLITHIATIC ACTIVITY

The hydroalcoholic extract of leaves of the plant in combination with the core stem of Musa paradisiaca and corn silk of Zea mays and the presence of bioenhancer like Pepper nigrum was evaluated by the invitro model. The anti-urolithiatic action of these polyherbal drug combinations in presence of bioenhancer was successfully evaluated and compared with the standard drug Cystone.[51] The Aqueous extract of K. pinnata leaves was utilized to explore the Antiurolithiatic activity by different in-vitro models. The extract of Kalanchoe pinnata exhibited inhibitory action in both nucleation and aggregation assays to a significant level52. The Ethylacetate fraction was separated from the hydroethanolic extract of K. pinnata for the quantitative analysis of total polyphenol and flavonoid content. Flavonoids can prevent the adhesion of CaOx crystals in the urinary tract by free-radical scavenging effects and stop further injury in the process of kidney stone formation extract with high flavonoid contents has been reported to have antilithiasis activity Polyphenols from grape seed extract prevented CaOx monohydrate induced papillary calculus formation.[53]

hydroalcoholic extract of K. pinnata was given orally to examine activity against sodium oxalate (NaOx) mediated urolithiasis, with Cystone (500 mg/kg, p.o.) as a standard. BPHE can help to avoid calcium oxalate crystal deposition in the kidney by preventing hyperoxaluria-induced peroxidative damage to the renal tubular membrane surface, which can lead to calcium oxalate crystal attachment and kidney stone formation. These results moreover showed that administering Bryophyllum pinnatum leaf hydroalcoholic extracts decreased and avoided the formation of urinary stones.[54] When twenty herbal hot aqueous leaf extracts for assessing their efficiency against urolithiasis in an experimental calcium oxalate-induced in vitro (chicken egg membrane) model. Among these screened herbal drugs Kalanchoe pinnata exhibited promising results compared to the standard chemical (potassium-magnesium citrate) and Phyto-formulation drug (cystone) for treating urolithiasis. The phytochemical profiling (qualitative and quantitative) and virtual studies indicated rutin from Kalanchoe pinnata as a probable contender for preventing kidney stones.[55] The antiurolithiatic activity of ethyl acetate extract of plant Kalanchoe pinnata was evaluated against ethylene glycol and ammonium chloride along with in vitro calcium oxalate (CaOx) crystals. Ethyl acetate fraction of K. pinnata showed a highly significant antilithiatic effect by increasing urine volume, normalizing disrupted urine parameters, increasing LDH level, and decreasing kidney tissue oxalate content. K. pinnata ethyl acetate fraction treatment showed a pronounced reversal of tubular dilation and damage of epithelial cells in kidney tissue with very less inflammatory cell infiltration.[56]

## ANTINEOPLASTIC ACTION

A chloroform extract derived from a bulk of botanically well characterized pulverized B. pinnata leaves was used to evaluate anti-cancer and anti-Human Papillomavirus (HPV) activities. B. pinnata crude leaf extract and all its

chromatographic fractions were examined for cell-growth inhibitory properties on HeLa cells. Cells treated with the indicated concentration of test sample were examined by MTT assay for the cell viability all these confirmed that B. pinnata can act as an anti-HPV molecule and apoptosis-inducing property. It, therefore, provides an important lead for the development of anti-cancer therapeutics for the management of cervical cancer.[57] From the aqueous extracts of leaves of K. Pinnata the flavonoids, quercetin, and rutin. Were obtained and evaluated phytochemically. The cytotoxic activity was evaluated in human carcinoma cell lines hep-2, Caco-2, and T84. In cell cultures of hep-2, the aqueous extract of leaves showed no toxicity. However, Caco-2 and T84 strains were more sensitive to the culture in the presence of the extract in a high concentration (1000 µg.ml-1). The flavonoids quercetin and rutin and the methanol at a concentration of 5% showed no toxicity for the cultivation of different cell lines evaluated. The cytotoxic activity of extracts of the species has been attributed to compounds called bufadienolides.[58] cytotoxicological and genotoxicological effects of Kalanchoe pinnata (Lam.) Pers. fresh leaf juice, for establishing a safe and effective quantity for use. Kalanchoe pinnata showed dose dependent changes in all the parameters. The 50 ml of juice showed a non significant increase in all the parameters studied. The 70 ml of juice also showed a non-significant increase in most parameters exceptMI, SCEs/Cell, and SCEs/Chromosome. This minor significant increase indicates that the juice at higher doses can cause potential genotoxic and cytotoxic effects. The two doses of K. pinnata fresh leafy juice used in our study were not found to possess a genotoxic potential and also proved as safe doses. Hence, they can be used pharmaceutically as well as traditionally but care should be taken for long durations and higher quantity use.[59]

## ANTIMICROBIAL ACTION

From the aqueous extracts of leaves of K. Pinnata the flavonoids, quercetin, and rutin. Were obtained and evaluated phytochemically. The antibacterial activity was evaluated by the macro dilution method. Quercetin is capable of inhibiting the bacterial growth of all tested strains. The results indicate the potential use of the species in the treatment of bacterial infections. The evaluation of the antimicrobial activity of the aqueous extract and flavonoids has been carried out by the method of agar dilution (microdilution). The aqueous extract of leaves showed a reduction in the growth of four of the evaluated strains. Quercetin has noted antibacterial activity at concentrations above 10 µg.mL-1 being able to inhibit the growth of all the strains tested in this study. Besides these strains, quercetin also presents antibacterial activity in strains of Proteus mirabilis, Acinetobacter baumannii, Helicobacter pylori, and also methicillin-resistant S. aureus (MRSA) when evaluated alone or in combination with oxacillin rutin demonstrated antibacterial activity for all tested strains. The most significant result for this flavonoid was held at the concentration of 100 µg.mL-1, with the reduction of all tested strains. In some strains, like E. coli and S. aureus, the minimum inhibitory concentration for rutin is presented in amounts exceeding 100 µg.mL-158. The extracts of K. pinnata (wild and transgenic) did not exhibit any cytotoxic activity towards the wound bed or general toxicity in animals in the applied concentration (1mL of the extract per dose, total protein concentration 1mg/mL) Water extract of wild-type K. pinnata exhibited both microbicides and wound healing activity, although it's own microbicide activity was lower than in Cefazolin. K. pinnata + CecP1 extract exhibited the same microbicide activity against S. aureus mono-infection as Cefazolin. The activity of K. pinnata + CecP1 extract against a combination of S. aureus and P. aeruginosa was much better than in Cefazolin.[60] K. pinnata water extracts containing cecropin P1 (CecP1). Wild-type K. pinnata extract exhibited evident microbicide activity against S. aureus with P. aeruginosa but it was substantially strengthened in K. pinnata + CecP1.[61]

## ANTIULCER ACTION

The hydroethanolic extract (HE) and ethyl acetate fraction (EAF) from Kalanchoe pinnata leave against an ethanol/HCL-induced ulcer model in rats. The HE reduced gastric lesions by approximately 47% (400 mg/kg). Significant inhibition of the gastric lesions by 50% was observed after pretreatment with the EAF (200 mg/kg). Quercetin and quercetin 3-O-α-L-arabinopyranosyl-(1→2)-α-L-rhamnopyranoside were isolated and identified in the flavonoid fraction (EAF) by HPLC and NMR analyses because this fraction showed the highest gastroprotective effect.[62]

## ANTIOXIDANT ACTION

Bhatti et al evaluate the total phenolic contents, flavonoid contents, and in vitro evaluation of antioxidant potentials by five different assay methods of various (benzene, chloroform, acetone,

and ethanol) extracts of leaves and stems of Kalanchoe pinnatum. The total phenolic compound was determined using the Folin-Ciocalteu method and the results were expressed as gallic acid equivalents or %w/w. The total flavonoid content was determined using the Dowd method in vitro evaluation of antioxidant potentials by DPPH scavenging activity. Phenolic and flavonoid content in leaves was found to be higher than stems in all the extracts and order: Ethanol >acetone > chloroform > benzene, which is further proved by in vitro antioxidant studies. Extracts contain a significant amount of phenolic and flavonoids and exhibit significant antioxidant activity through the scavenging free radicals which participate in various pathophysiology of diseases including ageing.[63] Mohan et al[64] examined the antioxidant activity of ethanolic extract of the leaves of the plant Kalonchoe pinnata. Screening models such as inhibition of lipid peroxidation, nitric oxide superoxide radical, and hydroxyl radical scavenging activity. Butylated Hydroxy Toluene (BHT) was used as a standard for anti-lipid peroxidation activity for nitric oxide Gallic acid was used as a standard, Ascorbic acid was used as the standard for superoxide anion radical scavenging activities, and mannitol was used as the standard for hydroxyl radical scavenging activity. The extract inhibits nitrite formation by directly competing with oxygen in the reaction with nitric oxide. The study proved that the extract studied has comparable nitric oxide scavenging activity with the standard gallic acid. The dried extract of Kalanchoe pinnata showed considerable inhibiting activity of in-vitro lipid peroxidation. the plant extract showed potent scavenger action of superoxide radical than the standard ascorbic acid mainly because of flavanoids. the plant extract showed better hydroxyl radical scavenging activity with an IC50 value of 4.64 µg/ml compared to an IC50 of 5.33 µg/ml of mannitol.

In vitro antioxidant activity of ethanol extract of leaves was studied using DPPH radical scavenging, reducing power determination assays. The extract displayed significant reducing power which was found to increase with the increasing concentration. IC50 values of DPPH scavenging activity was 282.136±0.46µg/ml.[65]

## HEPATOPROTECTIVE ACTION

The ethanolic extract of leaves showed considerable hepatoprotective action of plants against CCl4-induced hepatotoxicity in rats. decrease the serum bilirubin level by the plant extract up to 105.50% and decrease of SGPT level to 92.47 and 81.37%, respectively. These results strongly support the significant hepatoprotective activity of the drug showing the hepatoprotective activity of K. pinnata Pers. justifies the use of the juice of this plant in folk medicine for jaundice.[66]

## IMMUNOSUPPRESSANT ACTION

Ethyl acetate (FE) and n-butanol (FB) extract of plant K. pinnata showed immunosuppressant activity in tetramethylpentadecane (TMPD)-treated mice resulting in lupus-like disease mice with systemic immune imbalance. The ethyl acetate fraction of Kalanchoe pinnata has a higher immunosuppressant activity than the n-butanol fraction to repair the disorder that occurred in the TMPD-treated lupus mice.[67]

## ANTILEISHMANIAL ACTION

Santos et al reported that Kalanchoe pinnata contains substances potentially active and safe for the oral treatment of human cutaneous leishmaniasis. The safety of oral Kp was experimentally confirmed in mice treated with Kp doses higher than required for cure in murine leishmaniasis. oral Kp used efficiently inhibited the growth of active cutaneous lesions in a naturally infected case. Upon Kp, the fast-growing lesion stabilized and was 2 mm smaller at the end of the 14-day treatment. the fast therapeutic effect of Kp observed was due to an anti inflammatory effect of Kalanchoe due to proinflammatory factors such as IFN-γ and nitric oxide are important for fighting infection. the antileishmanial effect of Kp involves activation of nitric oxide intermediates in man68. Da Silva et al used BALB/c mice for the experiment and Leishmania amazons is (LMA) was used to induce the disease, the work demonstrates that the aqueous extract of plant protects mice against progressive infection with LMA by the oral route of administration.[45]

## ANTIASTHMATIC AND ANTITUSSIVE

Edward et al evaluate the antiasthmatic and antitussive properties of the aqueous leaf extract of Bryophyllum pinnatum study suggested that the aqueous leaf extract of B. Pinnatum may prevent the acute asthmatic attack in humans. the dose of 400 mg/kg/day for 21 days when compared with standard drug salbutamol 0.5 mg/kg/day protect guinea pigs from histamine induced convulsive dyspnea. This study also showed antitussive action of Bryophyllum pinnatum either central

or peripheral action wit reduction in the mucous secretion and viscosity and airflow resistance is reduced.[69]

## CONCLUSION

The present review shows the pharmacological potential, phytochemical analysis, and ethnobotanical uses of K. pinnata. A consolidated review on the pharmacological uses of the medicinal plant K. pinnata (Linn.) Pers. Which included a broad spectrum of activities like antidiabetic, nephroprotective, chemoprotective, anti histamine, antileishmanial, anthelmintic, insecticidal, anti-allergic, analgesic, immunosuppressive effects have been briefly discussed. Kalanchoe is rich in alkaloids, triterpenes, glycosides, flavonoids, steroids, and lipids. The leaves contain a group of chemicals called bufadienolides which are very active and have sparked the interest of scientists. They are very similar in structure and activity to two other cardiac glycosides, digoxin and digitoxin (drugs used for the clinical treatment of congestive heart failure and related conditions). The plant is traditionally known for its high clinical value s the plant can be explored for a clinical study.

## ABBREVIATIONS

*KP; Kalanchoe pinnata*, P.O.: Per orally, QE; quercetin, tetramethylpentadecane; TMPD.

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